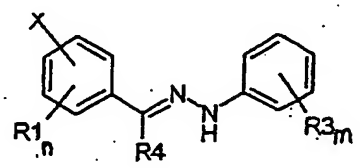
International Patent Application
No.PCT/EP03/00504
The Genetics Company Inc.
27196P WO/MDBCmh

New Claims

1. Beta-secretase inhibitor of formula (1)

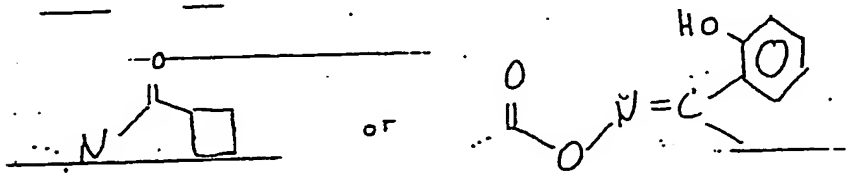


wherein

X: represents a halogen or a moiety which is bioisosteric thereto, in particular, F, Cl, Br, I, Methyl or CF_3, preferably Cl.

R1: each independently represents halogen, hydroxy, cyano, trifluoromethyl, nitro, a hydrocarbon group containing 1 to 4 carbon atoms, in particular, C1-C4 alkyl, C2-C4 alkenyl or C2-C4 alkynyl, which may be substituted, e.g. hydroxyalkyl, haloalkyl, cyanoalkyl, carboxyalkyl, acylalkyl, oxyalkyl, sulfonylalkyl, sulfonylamidoalkyl, amidoalkyl, carbonoylalkyl, ureylalkyl, etc. or a moiety which is bioisosteric thereto and n = 0 to 2.

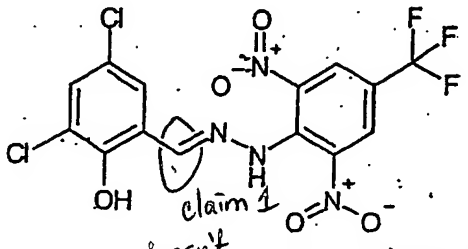
R3: each independently selected from R1 or is a aryl or heterocyclic moiety substituted by 0 to 4 moieties from R1 or a group selected from



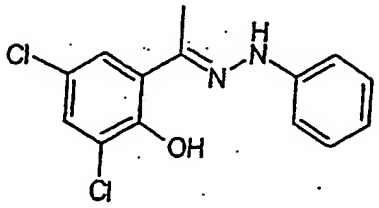
R4: represents halogen, hydroxy, cyano, trifluoromethyl, C1-C4 alkyl, C2-C4 alkenyl or C2-C4 alkynyl which may be substituted, e.g. hydroxyalkyl, haloalkyl, cyanoalkyl, carboxyalkyl, acylalkyl, oxyalkyl, sulfonylalkyl, sulfonylamidoalkyl, amidoalkyl, carbonylalkyl, ureylalkyl, etc. or a moiety which is biosteric thereto.

and m = 0 to 4.

2. Beta-secretase inhibitor according to claim 1 having the formula



or



claim 1 doesn't allow for hydrogen here (R4).

Search of claim 1 was constructed to include hydrogen as a definition for R4.

3. Beta-secretase inhibitor according to claim 1 or 2, having an IC50 ≤ 200 μM.

4. Beta-secretase inhibitor according to any of claims 1 to 3, being active in cells.

5. A pharmaceutical composition comprising a beta-secretase inhibitor according to any of claims 1 to 4, optionally in admixture with one or more pharmaceutically acceptable carriers, diluents and/or excipients.

6. A substance library containing at least 5 beta-secretase inhibitors according to any of claims 1 to 4.

7. The use of a beta-secretase inhibitor according to any of claims 1 to 4 for the manufacture of a pharmaceutical agent for the treatment or prevention of a condition which is mediated by beta-secretase.

8. The use of a beta-secretase inhibitor according to any of claims 1 to 4 for the manufacture of a pharmaceutical agent to inhibit the formation of beta amyloid peptides from the amyloid precursor protein (APP).

9. The use according to claim 7 or 8 for the manufacture of a pharmaceutical agent for the treatment or prevention of Alzheimer's disease or any disorder caused by pathological deposits of beta amyloid peptides.

10. Use of a beta-secretase inhibitor according to any of claims 1 to 4 in the manufacture of a pharmaceutical agent for the treatment or prevention of conditions selected from the group consisting of Alzheimer's disease, Down syndrome, cerebral amyloid angiopathy, Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch type (HCHWA-D) and other degenerative dementia characterized by beta-amyloid deposits.

11. A method of treating or preventing a disease characterized by beta-amyloid deposits such as Alzheimer's disease by modulating the activity of the beta-amyloid converting enzyme, comprising administering to a patient in need of such treatment a compound according to claims 1 to 4, or a pharmaceutically acceptable salt thereof.

12. Beta-secretase inhibitor having the formula